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L4	L3 and alle$ specific primer$1	13	L4
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☐ 1. 6391558 . 14 Apr 00; 21 May 02. Electrochemical detection of nucleic acid sequences. Henkens; Robert W., et al. 435/6; 422/50 422/62 422/63 422/67 422/68.1 422/69 422/82.01 435/91.1 435/91.2. C12Q001/68 C12P019/34 G01N015/06 G01N030/96 G01N027/00.

☑ 2. 6361949 . 22 Feb 00; 26 Mar 02. Nucleic acid amplification with direct sequencing. Sommer; Steven Seev. 435/6;. C12Q001/68 C12Q001/70.

☑ 3. 6322976 . 17 Mar 99; 27 Nov 01. Compositions and methods of disease diagnosis and therapy. Aitman; Timothy J., et al. 435/6; 435/7.23 536/23.1 536/24.3 536/24.31. C12Q001/68 G01N033/574 C07H021/02 C07H021/04 C07H021/00.

☑ 4. 6316198 . 18 Mar 00; 13 Nov 01. Detection of mutations in genes by specific LNA primers. Skouv; Jan, et al. 435/6; 435/91.1 435/91.2 536/23.1 536/24.3. C12Q001/68 C12P019/34 C07H021/02.

☐ 5. 6117635 . 11 Apr 97; 12 Sep 00. Nucleic acid amplification oligonucleotides with molecular energy transfer labels and methods based thereon. Nazarenko; Irina A., et al. 435/6; 435/91.2 536/22.1 536/24.33 536/25.32. C12Q001/68 C12P019/34 C07H021/04 C07H021/00.

☑ 6. 6090552 . 11 Jul 97; 18 Jul 00. Nucleic acid amplification oligonucleotides with molecular energy transfer labels and methods based thereon. Nazarenko; Irina A., et al. 435/6; 435/91.2 536/24.3 536/24.32 536/24.33. C12Q001/68 C12P019/34 C07H021/04 C12N015/00.

☐ 7. 6027913 . 27 Dec 94; 22 Feb 00. Nucleic acid amplification with direct sequencing. Sommer; Steven S.. 435/69.1; 435/91.21. C12P021/00 C12P019/34.

☑ 8. 6015670 . 14 Nov 97; 18 Jan 00. Methods for identifying a mutation in a gene of interest without a phenotypic guide using ES cells. Goodfellow; Peter N.. 435/6; 435/91.2. C12Q001/68 C12P019/34.

☐ 9. 5994075 . 16 May 97; 30 Nov 99. Methods for identifying a mutation in a gene of interest without a phenotypic guide. Goodfellow; Peter N.. 435/6; 435/441 435/444 435/446 435/91.2. C12Q001/68 C12P019/34.

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(L4 AND FLUORESCENCE).USPT,JPAB,EPAB,DWPI.	9

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=> s monitor?(10a)amplif?(10a)fluorescen?
L1          92 MONITOR?(10A) AMPLIF?(10A) FLUORESCEN?

=> s l1 and sequencing
L2           5 L1 AND SEQUENCING

=> s l2  and allel? specific primer#
L3           0 L2 AND ALLEL? SPECIFIC PRIMER#

=> s l1 and allel? specific primer#
L4           2 L1 AND ALLEL? SPECIFIC PRIMER#

=> s l4 and sequencing
L5           0 L4 AND SEQUENCING

=> d l4 1-2 bib ab

L4   ANSWER 1 OF 2     MEDLINE
AN   2000115340      MEDLINE
DN   20115340   PubMed ID: 10649496
TI   Mutation detection by TaqMan-allele specific amplification: application to
     molecular diagnosis of glycogen storage disease type Ia and medium-chain
     acyl-CoA dehydrogenase deficiency.
AU   Fujii K; Matsubara Y; Akanuma J; Takahashi K; Kure S; Suzuki Y; Imaizumi
     M; Iinuma K; Sakatsume O; Rinaldo P; Narisawa K
CS   Department of Medical Genetics, Tohoku University School of Medicine,
     Sendai, Japan.
SO   HUMAN MUTATION, (2000) 15 (2) 189-96.
     Journal code: 9215429. ISSN: 1059-7794.
CY   United States
DT   Journal; Article; (JOURNAL ARTICLE)
LA   English
FS   Priority Journals
EM   200002
ED   Entered STN: 20000309
     Last Updated on STN: 20000309
     Entered Medline: 20000224
AB   We have devised an allele-specific amplification method with a TaqMan
     fluorogenic probe (TaqMan-ASA) for the detection of point mutations.
     Pairwise PCR amplification using two sets of allele-
     specific primers in the presence of a TaqMan probe was
     monitored in real time with a fluorescence detector.
     Difference in amplification efficiency between the two PCR
     reactions was determined by "threshold" cycles to differentiate mutant and
     normal alleles without post-PCR processing. The method measured the
     efficiency of amplification rather than the presence or absence of
     end-point PCR products, therefore allowing greater flexibility in
     designing allele-specific primers and an
     ample technical margin for allelic discrimination. We applied the
     TaqMan-ASA method to detect a prevalent 727G>T mutation in Japanese
     patients with glycogen storage disease type Ia and a common 985A>G
     mutation in Caucasian patients with medium-chain acyl-CoA dehydrogenase
     deficiency. The method can be automated and may be applicable to the DNA
     diagnosis of various genetic diseases.
     Copyright 2000 Wiley-Liss, Inc.

L4   ANSWER 2 OF 2  BIOSIS  COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN   2000:113844  BIOSIS
DN   PREV200000113844
TI   Mutation detection by TaqMan-allele specific amplification: Application to
     molecular diagnosis of glycogen storage disease type Ia and medium-chain
     acyl-CoA dehydrogenase deficiency.
AU   Fujii, Kunihiro; Matsubara, Yoichi (1); Akanuma, Jun; Takahashi,
     Kazutoshi; Kure, Shigeo; Suzuki, Yoichi; Imaizumi, Masue; Iinuma, Kazuie;
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Sakatsume, Osamu; Rinaldo, Piero; Narisawa, Kuniaki
CS (1) Department of Medical Genetics, Tohoku University School of Medicine, 1-1 Seiryomachi, Aobaku, Sendai, 980-8574 Japan
SO Human Mutation, (2000) Vol. 15, No. 2, pp. 189-196.
ISSN: 1059-7794.
DT Article
LA English
SL English
AB We have devised an allele-specific amplification method with a TaqMan fluorogenic probe (TaqMan-ASA) for the detection of point mutations. Pairwise PCR amplification using two sets of **allele-specific primers** in the presence of a TaqMan probe was **monitored** in real time with a **fluorescence** detector. Difference in **amplification** efficiency between the two PCR reactions was determined by "threshold" cycles to differentiate mutant and normal alleles without post-PCR processing. The method measured the efficiency of amplification rather than the presence or absence of end-point PCR products, therefore allowing greater flexibility in designing **allele-specific primers** and an ample technical margin for allelic discrimination. We applied the TaqMan-ASA method to detect a prevalent 727G>T mutation in Japanese patients with glycogen storage disease type Ia and a common 985A>G mutation in Caucasian patients with medium-chain acyl-CoA dehydrogenase deficiency. The method can be automated and may be applicable to the DNA diagnosis of various genetic disease.

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L6 ANSWER 1 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:334723 BIOSIS
DN PREV200100334723
TI Methods and devices for hemogeneous nucleic acid amplification and detector.
AU Higuchi, Russell G. (1)
CS (1) San Francisco, CA USA
ASSIGNEE: Roche Molecular Systems, Inc.
PI US 6171785 January 09, 2001
SO Official Gazette of the United States Patent and Trademark Office Patents, (Jan. 9, 2001) Vol. 1242, No. 2, pp. No Pagination. e-file.
ISSN: 0098-1133.
DT Patent
LA English
AB This invention relates to improved methods for nucleic acid detection using methods such as the polymerase chain reaction (PCR). More specifically, the invention provides methods for simultaneous amplification and detection to enhance the speed and accuracy of prior methods. The methods involve the introduction of detectable DNA binding agents into the amplification reaction, which agents produce a detectable signal that is enhanced upon binding double-stranded DNA. In a preferred embodiment, the binding agent is a **fluorescent** dye. The methods also provide means for **monitoring** the increase in product DNA during an **amplification** reaction.
AB. . . produce a detectable signal that is enhanced upon binding double-stranded DNA. In a preferred embodiment, the binding agent is a **fluorescent** dye. The methods also provide means for **monitoring** the increase in product DNA during an **amplification** reaction.
IT Methods & Equipment
polymerase chain reaction [PCR]: DNA amplification, DNA amplification

method, detection method, in-situ recombinant gene expression detection, **sequencing** techniques, simultaneous amplification-detection

L6 ANSWER 2 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 2001:317029 BIOSIS
DN PREV200100317029
TI **Monitoring** of mixed chimerism by a technique using **fluorescence** based PCR **amplification** of microsatellite after allogeneic hematopoietic stem cell transplantation.
AU Saito, Akiko (1); Ogawa, Seishi (1); Hadama, Tohru; Kinoshita, Moritoshi; Chiba, Shigeru (1); Hirai, Hisamaru (1)
CS (1) Hematology and Oncology, University of Tokyo, Bunkyo-ku, Tokyo Japan
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 395a. print. Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB (Introduction) Monitoring of mixed chimerism following hematopoietic stem cell transplantation (HSCT) provides an important clue to evaluate engraftment and to detect graft failure or early relapse. Several techniques have been applied for this purpose; Mixed chimerism after sex-mismatched transplant can be quickly and quantitively assessed by fluorescent in situ hybridization (FISH) analysis using X- and Y-specific probes. Assessment of chimerism in sex-matched transplant has also been possible by differentially detecting a polymorphic allele(s) between the donor and recipient. However, the conventional methods for quantitive detection of polymorphisms such as VNTRs have been frequently too time-consuming in the contexet of clinical applications. In this study we intended to develop a simple method for quickly estimating post-transplant chimerism. (Materials and methods) Genomic DNA was extracted from bone marrow and/or blood samples of 27 donor-recipient pairs following allogeneic HSCT and subjected to the microsatellite PCR analysis, in which three microsatellite loci, D18S51, D20S471 and D22S684, were PCR-amplified using fluorescent primers from the genomic DNAs and length of the PCR products were analyzed using an ABI PRISM 377 automated sequence analyzer. Because the polymorphism in a given locus is represented by the difference in the length of the corresponding PCR products, we first determined the informative loci which showed different electrophoretic mobilities between the donor-recipient pair, and then assessed the chimerism in a given sample by measuring relative intensity of each polymorphic peak for the informative loci. Reliability of this assay was tested by measuring chimerism of the standard DNA samples whose donor/recipient-composition was already known, and by comparing the results with those obtained from other assays, for example, XY-FISH. (Results) In our method, 11 of 11 (100%) cases transplanted from unrelated donors and 13 of 16 (81%) cases from related donors had at least one informative microsatellite locus. Measurement of the standard DNA samples show a linear correlation between the measured values for donor-recipient ratios and the standardized values for the DNA composition. More than 10% of chimera can be stably detected, using as little as ten nanograms of sample DNA. In 11 patients, results from the microsatellite PCR showed excellent concordance with the data obtained from the conventional FISH analysis using X- and Y-specific probes and/or probes detecting tumor-specific translocations. (Conclusions) Fluorescent primer-based microsatellite PCR assay is a feasible, rapid and reliable technique for assessment of mixed chimerism after allogenic HSCT, even with minuscule samples.
TI **Monitoring** of mixed chimerism by a technique using **fluorescence** based PCR **amplification** of microsatellite after allogeneic hematopoietic stem cell transplantation.
IT . . .

hybridization [FISH]: diagnostic method; microsatellite PCR [microsatellite polymerase chain reaction]: DNA amplification, amplification method, fluorescence-based, in-situ recombinant gene expression detection, **sequencing** techniques

IT Miscellaneous Descriptors
chromosomal translocations: tumor-specific; electrophoretic mobility; engraftment; mixed chimerism; Meeting Abstract; Meeting Poster

L6 ANSWER 3 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:135568 BIOSIS
DN PREV199900135568
TI Identification of Leptospira biflexa by real-time homogeneous detection of rapid cycle PCR product.
AU Woo, T. H. S; Patel, B. K. C. (1); Cinco, M.; Smythe, L. D.; Norris, M. A.; Symonds, M. L.; Dohnt, M. F.; Piispanen, J.
CS (1) Sch. Biomol. Biomed. Sci., Fac. Sci., Griffith Univ., Nathan Campus, Brisbane, QLD 4111 Australia
SO Journal of Microbiological Methods, (Feb., 1999) Vol. 35, No. 1, pp. 23-30.
ISSN: 0167-7012.
DT Article
LA English
AB Sequence analysis of 16S rRNA genes extracted from nucleic acids databases enabled the identification of a Leptospira biflexa (L. biflexa) signature sequence, against which a reverse primer designated L613, was designed. This primer, when used in conjunction with a universal bacterial specific forward primer designated Fd1, enabled the development of a LightCyclerTM-based PCR protocol in which **fluorescence** emission due to binding of SYBR Green I dye to **amplified** products could be detected and **monitored**. A melting temperature (Tm), determined from the melting curve of the amplified product immediately following the termination of thermal cycling, confirmed that the product was that of L. biflexa. Agarose gel electrophoresis therefore was not necessary for identification of PCR products. The PCR protocol was very rapid, and consisted of 30 cycles with a duration of 20 s for each cycle with the monitoring of the melting curve requiring an additional 3 min. The whole protocol was completed in less than 20 min. The PCR protocol was also specific and enabled the identification of 18 strains of L. biflexa, whilst excluding 14 strains of L. interrogans and Leptonema illini. Two examples of its utility in improving work flow of a Leptospira reference laboratory are presented in this article. The use of a simple boiling method for extraction of DNA from all the members of the Leptospiraceae family DNA further simplifies the procedure and makes its use conducive to diagnostic laboratories.
AB. . . conjunction with a universal bacterial specific forward primer designated Fd1, enabled the development of a LightCyclerTM-based PCR protocol in which **fluorescence** emission due to binding of SYBR Green I dye to **amplified** products could be detected and **monitored**. A melting temperature (Tm), determined from the melting curve of the amplified product immediately following the termination of thermal cycling,. . .
IT . . .
analytical method, gel electrophoresis; DNA extraction: Isolation/Purification Techniques: CB, extraction method; LightCycler PCR [polymerase chain reaction]: DNA amplification, amplification method, **sequencing** techniques, in-situ recombinant gene expression detection
IT Miscellaneous Descriptors
nucleotide sequence

L6 ANSWER 4 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1999:219054 BIOSIS
DN PREV199900219054
TI Continuous fluorescent monitoring of rapid cycle polymerase chain

reaction.
AU Pritham, Gregory H.; Wittwer, Carl T. (1)
CS (1) Department of Pathology, University of Utah Medical School, 50 N. Medical Drive, Salt Lake City, UT, 84132 USA
SO Journal of Clinical Ligand Assay, (Winter, 1998) Vol. 21, No. 4, pp. 404-412.
ISSN: 1081-1672.
DT Article
LA English
SL English
AB Polymerase chain reaction (PCR) amplification and analysis can be performed rapidly. Indeed, both amplification and analysis can occur simultaneously in the same instrument in only 10-30 minutes. Rapid cycle PCR is possible because denaturation, annealing, and extension are fast reactions. Currently, cycling speeds are limited by instrumentation, not chemistry. If rapid cycle PCR is continuously monitored with a fluorimeter, amplification progress can be followed with double-stranded DNA specific dyes or resonance energy transfer probes of multiple designs. Initial template copy number can be determined by monitoring fluorescence once each cycle. Continuous monitoring of fluorescence within a cycle as the temperature is changing can be used to follow product or probe hybridization. Fluorescence melting curves immediately after amplification provide dynamic dot blots of hybridization for product identification or single base genotyping.
IT Methods & Equipment
fluorimeter: laboratory equipment; genotyping: analytical method; polymerase chain reaction: DNA amplification, analytical method, **sequencing** techniques, molecular genetic method, in-situ recombinant gene expression detection; rapid cycle polymerase chain reaction-continuous **fluorescent monitoring**: DNA **amplification**, **sequencing** techniques, molecular genetic method, analytical method, in-situ recombinant gene expression detection
IT Miscellaneous Descriptors
instrumentation; melting curves; mutations: detection; template. . .

L6 ANSWER 5 OF 5 BIOSIS COPYRIGHT 2002 BIOLOGICAL ABSTRACTS INC.
AN 1998:472877 BIOSIS
DN PREV199800472877
TI Fluorescence cross-correlation: A new concept for polymerase chain reaction.
AU Rigler, Rudolf (1); Foeldes-Papp, Zeno; Meyer-Almes, Franz-Josef; Sammet, Cyra; Voelcker, Martin; Schnetz, Andreas
CS (1) Dep. Med. Biophys., MBB, Karolinska Inst., S-17177 Stockholm Sweden
SO Journal of Biotechnology, (Aug. 12, 1998) Vol. 63, No. 2, pp. 97-109.
ISSN: 0168-1656.
DT Article
LA English
AB In this article we present a new concept for the detection of any specifically amplified target DNA sequences in multiple polymerase chain reactions (PCR) based on fluorescence correlation spectroscopy (FCS). The accumulation of double-stranded target DNA is **monitored** by the cross-correlated **fluorescence** signals provided by two **amplification** primers which are 5'-tagged with two different kinds of fluorophores (Rhodamine-Green and Cy5). Only the amplified target DNA sequence carrying both primers is observed. Its signal emerges from the background of non-incorporated or non-specifically incorporated primers. Down to 10-25 initial copy numbers of the template in the PCR compartment DNA can presently be detected. No external or internal standards are required for determining the size and the amplified copy number of specific DNA. The PCR amplification process is started with all ingredients in a single compartment (e.g. of a microtiter plate), in which amplification and measurement are performed. This eliminates the need for post-PCR purification steps. The homogeneous one-tube approach does not

depend on fluorescence energy transfer between the fluorogenic dyes. Thus, it does not interfere with the enzymatic amplification reaction of PCR and allows the continued use of different conditions for amplifying DNA. The results exemplified by PCR-amplified 217-bp and 389-bp target DNA sequences demonstrate that the analysis based on two-color fluorescence cross-correlation is a powerful method for simplifying the identification of targets in PCR for medical use. For this purpose, an instrument optimized for two-color excitation and detection of two-color emission has been developed, incorporating the principle of confocal arrangement.

AB. . . sequences in multiple polymerase chain reactions (PCR) based on fluorescence correlation spectroscopy (FCS). The accumulation of double-stranded target DNA is **monitored** by the cross-correlated **fluorescence** signals provided by two **amplification** primers which are 5'-tagged with two different kinds of fluorophores (Rhodamine-Green and Cy5). Only the amplified target DNA sequence carrying. . .

IT Methods & Equipment
polymerase chain reaction: DNA amplification, in-situ recombinant gene expression detection, **sequencing** techniques, molecular genetic method; two-color fluorescence cross-correlation spectroscopy: analytical method

IT Miscellaneous Descriptors
biotechnology

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